Testimony

Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives

The Environment and Human Health: The Role of HHS

Statement of

Linda Birnbaum, Ph.D., D.A.B.T., A.T.S.
Director, National Institute of Environmental Health Sciences, National Institutes of Health, and
Director, National Toxicology Program
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 9:30 a.m.
April 22, 2010

Mr. Chairman and distinguished members of the Subcommittee—I am pleased to appear before you today to present testimony on our current understanding of and research activities on environmental health. My name is Linda Birnbaum; I am the Director of the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health, as well as the National Toxicology Program (NTP).

Environmental health science is advancing at a tremendous rate. We are bringing all the new tools of biomedical science to bear on the fundamental questions of the effects of toxic substances on biological systems. These tools – genetics, genomics, proteomics, metabolomics, informatics, computational biology, just to name some of these new disciplines – give us new insights on how environmental effects happen in our bodies, but also technologies to improve testing procedures to provide better and more timely information for the use of our agency partners who are responsible for risk assessment and risk management.

Our understanding of chemical toxicity has been challenged by the new science of epigenetics, which is the study of changes to the packaging of the DNA molecules that influence the expression of genes, and hence the risks of diseases and altered development. Studies indicate that exposures that cause epigenetic changes can affect several generations.[1] This new understanding heightens the need to protect people at critical times in their development when they are most vulnerable.

[1] Anway MD, Cupp AS, Uzumcu M, Skinner MK (2005) Epigenetic transgenerational actions of endocrine disruptors and male fertility. Science 308:1466-1469

Related to the field of epigenetics is the key concept of "windows of susceptibility." Research in animals and humans shows that the developmental processes that occur at fetal and early life stages are especially vulnerable to disruption from relatively low doses of certain chemicals.[2][3][4] We first saw this in the case of lead and other metals, which we learned decades ago could harm neurological development as a result of fetal and childhood exposures. This concept also applies to hormonally active agents which disrupt the endocrine system. This is an active area of our research program. For example, NIEHS and NTP are funding important studies to fill the gaps in our knowledge about bisphenol A (BPA), a widely distributed, high production compound with many uses, including plastics, food can linings, bottle tops, water supply pipes, and thermal paper recycling . Our Center for Evaluation of Risks to Human Reproduction determined that there was "some concern" about effects to the brain, behavior and prostate gland in fetuses, infants, and children exposed to BPA.[5] We are now supporting an aggressive research effort to fill the research gaps in this area, especially concerning BPA effects on behavior, obesity, diabetes, reproductive disorders, development of prostate, breast and uterine cancer, asthma, cardiovascular diseases and transgenerational or epigenetic effects.

In our NIEHS Breast Cancer and Environment Research Program, co-funded with the National Cancer Institute, researchers are investigating whether windows of susceptibility exist in the development of the mammary gland, when exposures to environmental agents may impact the breast and endocrine systems that can influence breast cancer risk in adulthood.

---

[2] Rogan WR, Ragan NB (2003) Evidence of effects of environmental chemicals on the endocrine system in children. Pediatrics 112:247-252

[3] Dolinoy DC, Weidman JR, Jirtle RL (2007) Epigenetic gene regulation: Linking early developmental environment to adult disease. Reproductive Toxicology 23:297-307

[4] Committee on Environmental Health, American Academy of Pediatrics (1999) Pediatric environmental health, 2nd edition, pp 9-23

[5] http://www.niehs.nih.gov/news/media/questions/sya-bpa.cfm See "What does some concern mean?"

The joint NIEHS/EPA program of 14 Centers for Children's Environmental Health is expanding into new areas of research including birth defects, childhood cancer including leukemia, diabetes, pubertal development, and the developmental basis of adult disease. This research is directed towards additional children's environmental health issues such as epigenetics, transgenerational effects, diet, oxidative stress, and tissue sensitivity. The Children's Center program continues its mentoring and support of new investigators and also actively supports the engagement of new community groups involved in children's environmental health issues.

Environmental exposures are now also being implicated in the obesity epidemic[6][7]. NIEHS is supporting research on the developmental origins of obesity and the theory that environmental exposures during development play an important role in the current epidemic of obesity, diabetes, and metabolic syndrome. There are data showing weight gain in adult rats and mice following developmental exposure to a number of different chemicals,[8] which have been termed "obesogens" by some researchers. Thus, at NIEHS we find it may be useful to start thinking about obesity not just in terms of genetics and lifestyle, but also in terms of how early life exposure to these "obesogenic" chemicals might be setting the stage for us to gain weight later in life.

[6] Grun F, Blumberg B (2009) Endocrine disrupters as obesogens. Mol Cell Endocrinol 304:19-29
[7] Verhulst SL, Nelen V, Hond ED, Koppen G, Beunckens C, Vael C, Schoeters G, Desager K (2009) Intrauterine exposure to environmental pollutants and body mass index during the first 3 years of life. Environ Health Perspect 117:122-126.
[8] Iguchi T, Watanabe H, Ohta Y, Blumberg B (2008) Developmental effects: oestrogen-induced vaginal changes and organotin-induced adipogenesis. Int J Androl 31:263-268.

NIEHS is also helping lead the way to developing new environmental monitoring technologies. Determining actual levels of exposure for use in research, risk assessment, and risk management is an ongoing challenge, and NIEHS is actively pursuing many research approaches to help solve this problem and thus promote more accurate science and better decision making. For example, the NIEHS is supporting development and testing of a robot called PIPER[9] capable of mimicking children's floor activities while collecting better estimates of young children's exposure to indoor air pollutants (particulate matter, pesticides, allergens, endotoxins and airborne fungi). A study of asthma and indoor environmental contaminants is currently underway to test PIPER in the homes of 200 children. The study will compare measurements of particulates obtained by PIPER with those from standard adult height monitoring stations and examine their association with asthma symptoms.

At NIEHS we also recognize that the ultimate goal is to move our science into real-world applications to solve problems in communities. The NIEHS Superfund programs feature many examples of excellent environmental health research with real-world impact.[10] Our Superfund grantee at New York University (NYU) works for the mayor of Jersey City as a consultant on the city's chromium cleanup. In addition, he has provided assistance to a Merced, CA neighborhood on its cleanup of a chromium problem. Our NYU Superfund grant includes an outreach project in New Jersey with a major goal of building a partnership between NYU researchers and chromium impacted community members in Hudson County, the majority of which are Hispanic or African American. Such a partnership provides a pathway by which our Superfund researchers can reach communities that are concerned about possible chromium exposure. It is a

[9] Pretoddler Inhalable Particulate Environmental Robotic
[10] http://www.niehs.nih.gov/research/supported/srp/

full partnership where the community participates in the design of the project from its onset through its conclusion.

Another Superfund study from a group from Harvard, working in a population of pregnant women with relatively low arsenic exposures in Tar Creek, OK, showed that arsenic was associated with impaired glucose tolerance during pregnancy and therefore may be associated with increased risk of gestational diabetes.[11] Researchers from the Duke University Superfund group recently learned that exposure to fipronil, a new pesticide being introduced to replace organophosphates for both household and agricultural use, results in the same adverse effects on neurodevelopment as chlorpyrifos. They also showed that the metabolic alterations evoked by early-life exposure to compounds often classified as "developmental neurotoxicants" support the idea of the potential involvement of environmental contaminants in the dramatic increase in childhood obesity and diabetes.[12][13]

With our rapidly increasing understanding of the subtleties of biological effects of environmental exposures, we are poised to move forward into an era of a new kind of toxicological testing that is less expensive and time-consuming than our current methods, and also gives us an improved understanding of the actual effects on humans. Toxicology is advancing from a mostly descriptive science using disease-specific models to a better predictive science focused upon a

[11] Adrienne S. Ettinger, Ami R. Zota, Chitra J. Amarasiriwardena, Marianne R. Hopkins, Joel Schwartz, Howard Hu, and Robert O. Wright. 2009. Maternal Arsenic Exposure and Impaired Glucose Tolerance during Pregnancy. *Environmental Health Perspectives* 117(7): 1059-1064.
[12] Slotkin, Theodore A. and Fredric J. Seidler. 2009. Protein kinase C is a target for diverse developmental neurotoxicants: transcriptional responses to chlorpyrifos, diazinon, dieldrin and divalent nickel in PC12 cells. *Brain Research* **1263:**23-32.
[13] Slotkin, Theodore A., Bethany E. Bodwell, Edward D. Levin, and Fredric J. Seidler. 2008. Neonatal exposure to low doses of diazinon: long-term effects on neural cell development and acetylcholine systems. *Environmental Health Perspectives* **116(3):**340-8.

broad inclusion of target-specific, mechanism-based, biological observations. This means using alternative assays targeting the key pathways, molecular events, or processes linked to disease or injury, and incorporating them into a research and testing framework. The NTP is laying the foundation for this testing paradigm in partnership with the National Human Genome Research Institute, EPA, and soon, FDA. They are using quantitative high-throughput screening assays to test a large number of chemicals. The resulting data are being deposited into publicly accessible relational databases. Analyses of these results will set the stage for a new framework for toxicity testing.

In summary, understanding the connection between our health and our environment, with its mixture of chemicals, diet and lifestyle stressors, is no less complex than understanding the intricacies of the human genome. At NIEHS, we remain committed to leading the evolution of the field of environmental health sciences to meet emerging public health challenges.

Mr. Chairman and members of the Subcommittee, thank you for giving me the opportunity to present testimony on this important issue. I would be happy to answer any questions.